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Microlamp for *in-situ* Tissue Spectroscopy for the Dosimetry of Photodynamic Therapy

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Abstract

Photodynamic therapy (PDT) is a growing treatment modality for various diseases, most notably cancer. It has several advantages compared to radiotherapy and chemotherapy, but a good dosimetry is very important for an efficient treatment. One of the key parameters in PDT dosimetry is oxygen availability in tissue, which can be measured making use of spectroscopic techniques. For this purpose, a broadband source is needed to illuminate the volume of interest at all wavelengths necessary for the spectroscopic information. In an implantable system under development, this broadband source is being implemented as a microfabricated lamp. In this paper we report on the characterisation of a tungsten microheater as the incandescent filament, showing that this type of element can be brought to emit significant radiation in the wavelength range of interest.

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Keywords: Microheater; tissue spectroscopy; photodynamic therapy; broadband light source; tungsten filament.

1. Introduction

Photodynamic therapy (PDT) is an expanding medical treatment [1] used for a variety of affections, ranging from acne to cancer. It shows great promise in this last field, as it offers important advantages compared to established treatment modalities. The local nature of its action and the fact that it does not cause cumulative damage to tissue are perhaps its most important qualities.

PDT consists of administering a light sensitive drug (photosensitiser) to the patient and using optical sources to excite it in the volume of interest, producing local damage to the malignant tissue. PDT has found application in situations where the tissue is accessible, but it has a lot of potential for other treatments where light cannot be injected from outside of the body. Within this context, we have developed an implantable system, see Figure 1 and

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2, that is able to deliver the light excitation using telemetric power and communications [2]. Using this device, new cancer modalities could be addressed, such as brain cancer.

The effect of PDT is highly dependent on three factors: the availability of oxygen, the presence of the drug and the amount of illumination. These parameters vary fast over space and time, making accurate dosimetry an important and difficult issue. Tissue spectroscopy provides data that can be used for measuring the availability of oxygen in tissue. The working principle is based on the different spectra of oxy- and deoxyhemoglobin, which can be fitted to measurements to obtain their concentrations. For this, the absorption coefficient has to be obtained at different wavelengths. Therefore, a broadband source and spectrographic detection are required.

In a first step towards the fabrication of the source, we are working on a tungsten filament that can be used as a black-body emitter with significant power in the wavelength range of interest (650nm-1000nm). Tungsten is used because of its good high-temperature properties. In this paper, we report on the characterisation of this element as its temperature increases. We have used finite element modelling and measurements to study its structural behaviour. We have determined that the maximum attainable temperature is 1420K from pyrometer measurements, which already offers useful power emission at the desired wavelengths. Future work will include optimization of the filament design for higher temperatures and encapsulation in a protective atmosphere for incorporation into the implantable system.

2. Background and fabrication steps

A light source can be used for tissue spectroscopy because when the emitted photons reach the tissue, some of them are scattered, others are absorbed and the rest are reflected. These effects are wavelength dependent and in consequence the tissue changes the emitted light spectrum. Which wavelengths are affected by one effect or another depends on the type of tissue. Therefore, it is possible to collect the reflected light and then, with this, get information about the tissue response to the emitted light. Moreover, the light reflected from the tissue has to be collected in the implant and then processed. Photodiodes are devices that are generally used to collect light and transform it into photocurrent. But the information that can be extracted from the photocurrent is not enough to get an accurate tissue characterisation. However, the modulation of the spectrum of the emitted light in combination with the addition of a few number of dielectric filters has shown a better tissue restoration [3]. This modulation of the emitted spectrum can be attained with the variation of the colour temperature of the incandescent filament of a microlamp [4]. This solution for the spectroscopy problem was modelled in Matlab. The results achieved in the simulations set useful specifications for the light source device. One of the critical specifications of the light source is the maximum temperature that this device can reach. Concretely, 2000K was the maximum temperature suggested in the theoretical calculations for a wavelength range between 650nm-1000nm. Although higher temperatures lead to better tissue restoration, the improvement above 2000K is not remarkable.

The broadband light source consists in a tungsten filament deposited over a silicon nitride membrane. Silicon nitride is frequently used in the fabrication of membranes because of its mechanical strength [5]. The fabrication steps are described in Figure 3. First, a layer of 200nm of silicon dioxide is grown using a wet thermal oxidation. Then, 500nm of low-stress silicon nitride is deposited on top. After, the low-pressure chemical vapour deposition of the nitride, a layer of chromium and then a layer of tungsten are sputtered and lifted off. Afterwards, holes for TEM imaging are defined (as originally we tried to estimate the deflection of the fabricated membrane by TEM). Finally, a window from the back side of the membrane is etched to expose the oxide and the silicon to a KOH solution. This wet etching removes the oxide and the silicon and stops in the front side nitride. The membrane is created and released after the KOH solution.

3. Results and discussion

We used finite element analysis to simulate the behaviour of the microfabricated heater. The maximum temperature reached in the simulations was 1428 Kelvin, see Figure 4. The expected deflection of the membrane at the maximum temperature achieved during the simulations is around 10µm. The maximum temperature that our light source can achieve was measured with a disappearing filament pyrometer. In this experiment, the colour of the tungsten filament inside the pyrometer was compared to the colour of the tungsten filament of the microheater to determine its temperature. Specifically, the maximum temperature determined with this method was 1420K. From these

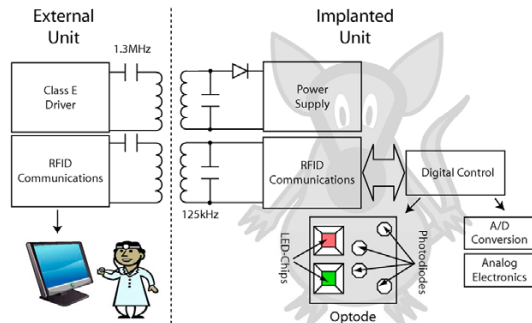


Figure 1: Schematic overview of the implantable PDT system

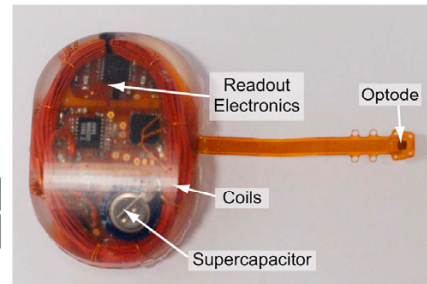


Figure 2: Implant for telemetric PDT showing the electronics, readout and the optical activation element

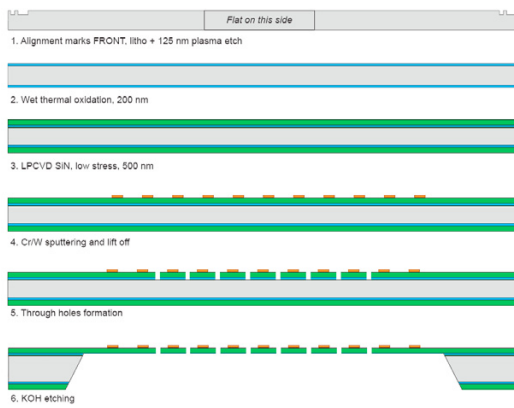


Figure 3: Fabrication steps of the microfabricated heater

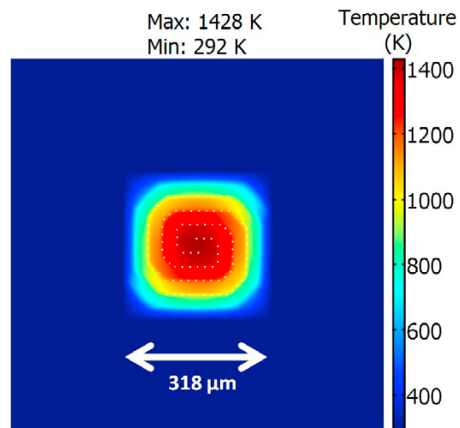


Figure 4: FEM study of the filament area, showing the expected deflection



Figure 5: Microheater at incandescent temperature. The maximum temperature being estimated to be 1420 K

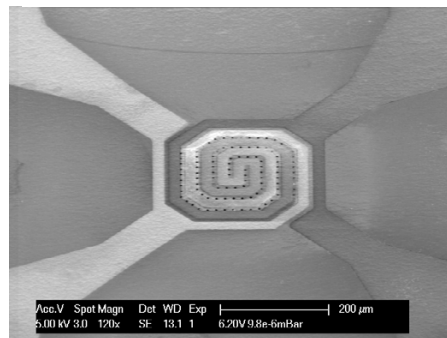


Figure 6: SEM picture of the microheater during operation

results, it is possible to say that the maximum attainable temperature of the microfabricated heater is above 1400K. Figure 5 shows the light source under study emitting visible light. Figure 6 is a SEM picture of the tungsten filament under operation in vacuum.

We used a white light interferometer to measure the deflection of the micromachined heater during operation. The surface of the membrane is scanned with the light interferometer to obtain a surface profile. The tungsten filament of the micromachined lamp was not yet encapsulated to protect it against oxidation. In addition, this experiment was performed under ambient conditions and for this reason we only measure the deflection for relatively low temperatures. Moreover, bulk tungsten starts to oxidise around 400 °C and above 700 °C the oxidation rate increases rapidly [6]. We observed that the deflection of the membrane for temperatures below 700 °C was in the micrometer order with a maximum of 5 μm . It is important to keep the deflection as low as possible because the induced thermo-mechanical stresses may cause the instability of the membrane and its rupture.

4. Conclusions

We have developed an implantable system to be used in photodynamic therapy. This implant is able to deliver a light excitation using telemetric power and communications. One of the key parameters for the success in the application of the PDT is the availability of oxygen in tissue. The presence of oxygen can be detected by means of a broadband light source and spectrographic detection. Furthermore, the absorption coefficient of the oxy- and deoxyhemoglobin at different wavelengths provides enough information to detect the presence of oxygen in tissue. In this paper, we focused in a light source capable of emitting light in the range of interest (650nm-1000nm) to do tissue spectroscopy. In previous studies we discovered that the optimum maximum temperature for the light source is 2000 K. In the present study, the high temperature microheater used as a microfabricated lamp reached approximately a maximum temperature above 1400K and a maximum deflection of the membrane around 10 μm . We have shown that both finite element calculations and measurements are similar. The temperature achieved with the microheater can be already used for tissue spectroscopy. In addition, the device should work in vacuum to avoid oxidation and to reach higher temperatures. In the future, the microfabricated lamp will include an optimization of the filament design for higher temperatures and an encapsulation in a protective atmosphere to avoid the oxidation of the filament. We achieved 2000K making use of a free standing tungsten filament, but we need a thicker filament to keep the mechanical stability with this solution. However, an increase in thickness means an increase in power consumption. Thus, there is a trade-off between filament thickness and power consumption that has to be solved.

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